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09/603,024	06/23/2000	Markus Pompejus	BGI-131CP	1349

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/603,024	POMPEJUS ET AL.	
	Examin r	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sh et with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 39-54 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of nucleic acids which encode a protein termed MCT, or portions thereof, in the specification, of SEQ ID NO: 1.

Credible Utility

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The cited utilities in the specification include modulation of chemical production and using the proteins to produce fine chemicals. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are utilities for the nucleic acid of SEQ ID NO: 1 which are identified in either the specification or in the cited prior art.

Substantial utility

Given the absence of a well established utility, the next issue is whether substantial utilities are disclosed in the specification. Here, the evidence in the specification provided is that the protein is related to the ABC transporter family of proteins. This relationship lacks any of the hallmarks of utility. The homology does not

imply that the proteins are similar in any function way, or that they are expressed in similar tissue types or under similar conditions. There is no biological activity, expression pattern, phenotype, disease or condition, ligand, binding partner or any other specific feature which is disclosed as being associated with the protein encoded by SEQ ID NO: 1. Without any further information, there is no expectation that the protein will have any properties in common with the ABC transporter protein. There is an abundance of evidence that very similar proteins can perform very different functions. For example, Rost et al (J. Mol. Biol. (2002) 318(2):595-608) notes regarding assignment of enzymatic activity based upon homology comparisons that "The results illustrated how difficult it is to assess the conservation of protein function and to guarantee error-free genome annotations, in general: sets with millions of pair comparisons might not suffice to arrive at statistically significant conclusions (abstract)." Thus, even high levels of homology do not necessarily correlate with actual protein function. In the current case, where the function of MCT (SEQ ID NO: 1) is not known, the expectation is even lower that there is any utility that can be derived based upon this association.

This situation is extremely similar to example 12 of the Utility Guidelines, where a protein which was known to be a receptor, but where the ligand was unknown, was found to lack utility. In the current case, the putative MCT protein, as an ABC transporter, lacks a known ligand. As shown in the prior art rejection in the previous action, the sequence was 74% identical to an ABC transporter, but had no specific function. Similar to the receptor in Example 12, it lacks a substantial utility because

there is no "real world" context of use. The only uses are unspecified methods of making the protein or methods of producing undefined and unnamed fine chemicals using the protein. Further research would be required to identify and reasonably confirm a "real world" context of use. As noted in the utility guidelines, basic research on a product to identify properties and intermediate products which themselves lack substantial utility are all insubstantial utilities (see page 6 of the Utility guideline training materials).

Specific Utility

In the current case, even if the substantial utility argument above were found unpersuasive, there is no specific utility given for this MCT protein of SEQ ID NO: 1 and the resultant nucleic acid. The protein has not been associated with any disease, any condition, or any other specific feature. The only association is that it has some homology to a protein, the ABC transporter. As the utility guideline training materials note on page 5-6, "Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed". Here, the homology to the ABC transporter gives no specific utility because ABC transporters represent a class of molecules which may export or import any of a variety of molecules ranging from lipids, polysaccharides and proteins to maltose or histidine (see Nikaido et al (PNAS (2002) 99(15):9609-9610). The class ranges to include a bacterial histidine transport protein and the human Cystic Fibrosis transmembrane conductance regulator (see Nikaido et al (PNAS (2002)

99(15):9609-9610). Therefore, there is no specific utility for this protein until a specific ligand is identified.

Finally, with regard to the utility analysis, the current situation directly tracks Examples 4 and 12 of the utility guidelines, where a protein of entirely unknown function and a receptor with an unknown ligand was characterized as lacking utility.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 43-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification, since the claims are not limited to any particular SEQ ID NO, but are open to a nucleic acid which encodes any protein 90% identical to SEQ ID NO: 1. The claims are further open to any nucleic acid which encodes any portion of the MCT protein of SEQ ID NO: 1 based on the fragment language. Most significantly, the genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID No 1. Thus, applicant has express possession of only one particular sequence in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains.

There is no showing or evidence which links structural limitations or requirements to any particular functional limitations. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acids as encoding an MCT protein that is 90% identical to SEQ ID NO: 1lacks any specific structure, since it is in the absence of knowledge of the material composition.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound without identifying the structure function relationship of the compound, so that the compound is claimed solely by the functional utility of being a nucleic acid which is 90% identical to SEQ ID NO: 1 without any additional structural limitations and without any functional limitations as required by the written description guidelines.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise SEQ ID NO 1.

Further, the claims fail to meet the written description guidelines on at least two grounds. First, there is no function associated with the sequence. Second, the 90% language does not specifically delimit what structural elements of the sequence are associated with the function. Thus, reviewing any of the DNA written description guidelines supports a finding that the current claims fail. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 – Scope of Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a nucleic acid which encodes the MCT protein. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass not only the particular MCT encoding nucleic acid but also include any nucleic acid which shares that name, any portion of the protein, or 50% homology thereto.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the activity of polypeptides and nucleic acids. It would require significant study to identify the actual function of the MCT protein and nucleic acid, and

identifying a use for this protein would be an inventive, unpredictable and difficult undertaking in itself. This would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art is extremely unpredictable with regard to protein function in the absence of reliable information regarding the protein activity. Even very similar proteins, as shown by homology, may have very different functions (see Rost et al (J. Mol. Biol. (2002) 318(2):595-608). In the current case, where no specific information is known regarding the function of the protein in actual biological organisms, it is entirely unpredictable what function and activity will be found for this protein. The prior art does not resolve this ambiguity, since no prior art activity is identified for the protein.

Working Examples

The specification has no working examples.

Guidance in the Specification.

The specification provides no specific or substantial uses for the MCT protein. The specification does generically teach that the protein may be used in the production of fine chemicals but no specific chemical is identified, no specific ligand for the MCT protein is identified and no specific resulting product is identified.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the issue of the efficacy of the control and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

6. The rejection of claims under 35 U.S.C. 102(b) is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 103

7. The rejection of claims under 35 U.S.C. 103(a) is withdrawn in view of the amendment.

Response to Arguments

8. Applicant's arguments filed December 29, 2003 have been fully considered but they are not persuasive.

Applicant first argues the utility rejection by attempting to rely upon two separate utilities. First, the function as a ATP transporter and second as useful in modulation of the synthesis of "fine chemicals". However, the first problem with these utilities is that Applicant does not know what is being transported. Assuming that the protein is, in fact, some sort of ABC transporter, it's ligand is unknown. As the Nakaido reference

makes clear, there is a tremendous variation in the ligands and consequent substantial utilities for proteins in the ABC transporter family.

There is no evidence in the specification regarding what this protein actually does. Thus, evidence regarding the activity or function of SEQ ID NO: 1 does not provide any significant evidence for it's substantial and specific patentable utilities. So the utility claimed by Applicant is the limited structural analogy to a different protein , ABC transporters, some of which may have utility. This is lesser level of utility than the amount rejected by the Supreme court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966). In Brenner, a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. So unlike in the current case, the related compound had a clear utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a polynucleotide encoding a protein which has no identified activity. The function of SEQ ID NO: 1 and its resulting protein are as yet undetermined with no known function or biological significance. Until some actual and specific significance can be attributed to SEQ ID NO: 1 as identified in the specification, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date directly consistent with *Brenner v. Manson*.

Applicant further argues that this case meets the requirements of MPEP 2164.07. Applicant is incorrect. The current case is significantly different and fails to comply with the utility guidelines because there is no listed function for the related protein, and there is no expectation of any particular utility for SEQ ID NO: 1. Further, the reliance on the homology to another protein underlies the fundamental problem in this application. The homology is to a large family of diverse and functionally divergent proteins. There is no evidence or teaching that SEQ ID NO: 1 has any of the activities found in the family of proteins. This protein has no utility because there is no known "real world" use for the protein. Applicant has not provided any such "real world" use.

The question at issue is whether or not the broad general assertion that the claimed nucleic acids of SEQ ID NO: 1 have utility where they might be used for *some* application but where the specification completely fails to identify *which* application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria and lacks

utility. *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.'). This is precisely the attempt of this Applicant. This Applicant is attempting to induce the office into a guessing game in which the actual use of SEQ ID NO: 1 will be determined by someone else, and from whom this Applicant will then attempt to extract payment once a "real world" use is identified.

So contrary to Applicant's arguments, the patent statue, as interpreted by the Supreme Court in Brenner v. Manson, requires specific benefit in currently available form. No such specific benefit is present in this case.

Applicant then argues the written description rejection. With regard to claims 39-42, these claims comply with the written description guidelines. However, claims 43-54 do not comply. Applicant's reliance on Example 14 is incorrect. In example 14, the identity was 95% and the current claims are significantly broader and permit 90% identity, which is a significantly broader claim. Second, in Example 14, there is a correlative function which is precisely defined and where the elements of the protein associated with the function are known. So that when the prediction of structural

identity is made, the combination of the function and the known regions of conservation render the protein somewhat predictable. These elements are all missing from the current claims. Applicant does not include any function in the claim, which alone distinguishes the claims from example 14. Further, Applicant does not use the more stringent 95% identity. This is significant because of the difference in genus sizes between 90 and 95% without any limitation based upon defined structural elements. In applicant's case, for SEQ ID NO: 1, which is 894 nucleotides long, 95% would permit a change in 44 nucleotides. However, this is worse than example 14, where conserved regions of protein function must be protected in order to retain catalytic function, only a limited set of the total sequence will be available for mutation. Here, no information regarding function is in the claim as in Example 14. Also unlike Example 14, no prior art information on routine mutations is available. So it is entirely undescribed and unknown what changes could be made and Applicant does not have possession of this genus. Therefore, the written description rejection is maintained.

With regard to the fragment claims, these are open "comprising" claims which read on full length genes which are not described. Unlike Example 15, the oligonucleotides do not have any function. So the analogy to example 15 is simply misplaced and the rejection is maintained.

With regard to the enablement rejection, this issue tracks the utility. In the absence of utility, the claimed invention cannot be useful. Applicant has not provided such a use since it is entirely unpredictable what function this protein will have, given

the divergent functions in the ABC transporter family. Therefore, this rejection is maintained.

As noted, the prior art rejections are withdrawn in view of the amendment.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
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